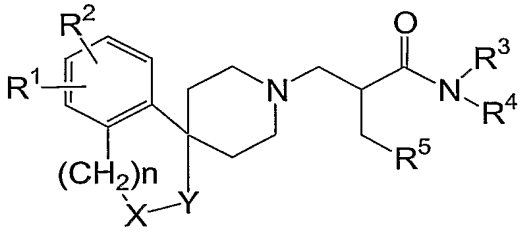
CLAIMS

1. A compound of the following formula (I)



(I)

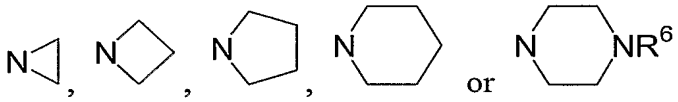
or a pharmaceutically acceptable ester of such a compound, or a pharmaceutically acceptable salt and solvates thereof, wherein

R^1 and R^2 independently represent a hydrogen atom, a halogen atom or an alkyl group having from 1 to 3 carbon atoms;

R^3 represents a hydrogen atom, a cycloalkyl group having from 3 to 6 carbon atoms, a tetrahydrofuranyl group, a tetrahydropyranyl group, or an alkyl group having from 1 to 6 carbon atoms, which alkyl group is optionally substituted by 1 to 3 groups selected from a cyano group, a halogen atom, a hydroxy group, an alkoxy group having from 1 to 3 carbon atoms, an oxo group, an amino group and a mono- or di- alkylamino group having from 1 to 3 carbon atoms;

R^4 represents a hydrogen atom or an alkyl group having from 1 to 3 carbon atoms; or

 represents one of the following



optionally substituted by 1 to 2 groups selected from an oxo group, a hydroxy group, a hydroxyalkyl group having from 1 to 3 carbon atoms, an alkoxy group having from 1 to 3 carbon atoms, an alkyl group having from 1 to 6 carbon atoms or an alkoxyalkyl group ahving a total of from 2 to 6 carbon atoms;

R^5 represents an aryl group having from 6 to 10 ring atoms or a heteroaryl group and said heteroaryl group is a 5- to 10-membered hetero aromatic group containing from 1 to 3 hetero atoms selected from a oxygen atom, a sulfur atom and a nitrogen atom;

said aryl group and heteroaryl group are optionally substituted by 1 to 3 groups selected from a halogen atom, a hydroxy group, an alkyl group having from 1 to 3 carbon atoms, an alkoxy group having from 1 to 3 carbon atoms, an alkyl group having from 1 to 6 carbon atoms interrupted by an oxgen atom, a hydroxyalkyl group having from 1 to 3 carbon atoms, an amino group, a mono-or di-alkylamino group having from 1 to 3 carbon atoms, an aminocarbonyl group, a mono- or di-alkylaminocarbonyl group having from 1 to 3 carbon atoms in each alkyl group, an alkanoylamino group having from 1 to 3 carbon atoms and an alkylsulfonylamino group having from 1 to 3 carbon atoms;

R^6 represents a hydrogen atom, an alkyl group having from 1 to 3 carbon atoms, an alkanoyl group having from 1 to 3 carbon atoms or an alkylsulfonyl group having from 1 to 3 carbon atoms;

-X-Y- represents a group of the formula $-N(R^7)C(=O)-$, $-C(=O)N(R^7)-$, $-N(R^7)CH_2-$, $-CH_2N(R^7)-$, $-N(R^7)SO_2-$, $-SO_2N(R^7)-$, $-CH_2CH_2-$, -CH=CH-, $-CH(CH_2OH)CH_2-$, $-CH_2CH(CH_2OH)-$,$-CH_2CH(OH)-$, $-CH(OH)CH_2-$, $-C(R^7)(R^8)-O-$ or $-O-C(R^7)(R^8)-$

R^7 represents a hydrogen atom or an alkyl group having from 1 to 3 carbon atoms;

R^8 represents a hydrogen atom, an alkyl group having from 1 to 3 carbon atoms or a hydroxyalkyl group having from 1 to 3 carbon atoms;

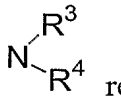
n represents an integer 0, 1 or 2

2. A compound according to Claim 1, wherein R^1 and R^2 independently represent a hydrogen atom or a fluorine atom.

3. A compound according to Claim 1 or Claim 2 wherein,

R^3 represents a hydrogen atom, a tetrahydrofuranyl group, an alkyl group having from 1 to 6 carbon atoms optionally substituted by 1 to 3 groups selected from a cyano group, a halogen atom, a hydroxy group, an alkoxy group having from 1 to 3 carbon atoms, an oxo group and a di- alkylamino group having from 1 to 3 carbon atoms; and

R^4 represents a hydrogen atom or an alkyl group having from 1 to 3 carbon atoms; or



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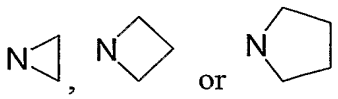
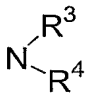


optionally substituted by 1 to 2 groups selected from a hydroxy group, a hydroxyalkyl group having from 1 to 3 carbon atoms, an alkoxy group having from 1 to 3 carbon atoms, an alkyl group having from 1 to 3 carbon atoms or an alkoxyalkyl group ahving a total of from 2 or 3 carbon atoms.

4. A compound according to any one of claims 1 to 3, R^3 represents a hydrogen atom, a tetrahydrofuranyl group, an alkyl group having from 1 to 6 carbon atoms optionally substituted by 1 substituent selected from a cyano group, a trifluoromethyl group, a hydroxy group, a methoxy group, an oxo group and a dimethylamino group; and

R^4 represents a hydrogen atom or a methyl group; or



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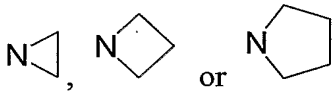
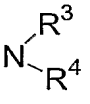


optionally substituted by 1 to 2 groups selected from a hydroxy group, a hydroxymethyl group, a methoxy group, a methyl group and a methoxymethyl group.

5. A compound according to any one of claims 1 to 4 wherein

R^3 represents a hydrogen atom, a tetrahydrofuranyl group, a methyl group, an hydroxyethyl group, a methoxybutyl group, a hydroxybutyl group, a methoxyethyl group, a hydroxypentyl group, a hydroxypropyl group, a cyano methyl group, a cyanomethyl group, a dimethylaminobutyl group, a trifluoroethyl group or a dimethylaminoethyl group; and

R^4 represents a hydrogen atom or a methyl group; or



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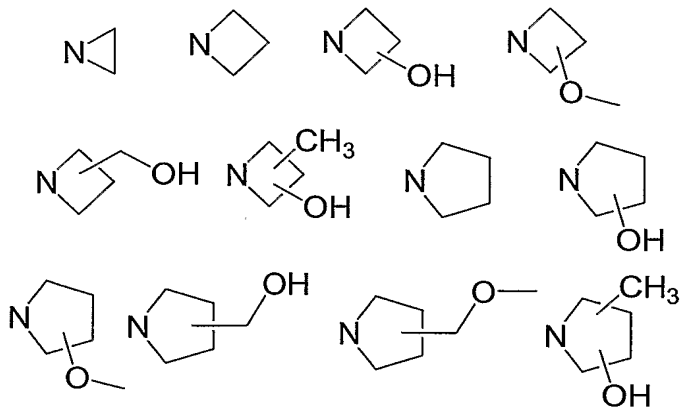

6. A compound according to any one of claims 1 to 5 wherein

R^5 represents a phenyl group or a heteroaryl group and said heteroaryl group is a 5- to 6-membered hetero aromatic group containing from 1 to 2 nitrogen heteroatoms or 1 or 2 nitrogen heteroatoms and 1 oxygen or 1 sulfur atom;

said phenyl group and heteroaryl group are optionally substituted by 1 to 3 groups selected from a halogen atom, a hydroxyl group, an alkyl group having from 1 to 3 carbon atoms, an alkyl group having from 1 to 6 carbon atoms interrupted by an oxgen atom, a hydroxyalkyl group having from 1 to 3 carbon atoms, an amino group and an alkylsulfonylamino group having from 1 to 3 carbon atoms.

7. A compound according to any one of claims 1 to 6 wherein

R^5 represents a phenyl group or a heteroaryl group selected from a pyridyl group, a thiazolyl group, a pyrazolyl group and an oxazolyl group;

said phenyl group is optionally substituted by 1 to 3 groups selected from a fluorine atom, a chlorine atom, a hydroxy group, a methyl group, a methoxymethyl group, a hydroxymethyl group, an amino group and methanesulfonylamino.

8. A compound according to any one of claims 1 to 7, wherein

-X-Y- represents a group of the formula $-N(CH_3)C(=O)-$, $-N(CH_3)CH_2-$, $-N(CH_3)SO_2-$, $-CH_2O-$, $-CH(CH_3)O-$, $C(CH_3)_2O-$, $-CH(CH_2OH)O-$, $-CH_2CH_2-$, $-CH(CH_2OH)CH_2-$, $-CH(OH)CH_2-$, -CH=CH-, or $-CH_2CH(OH)-$.

9. A compound according to any one of claims 1 to 8, wherein

-X-Y- represents a group of the formula $-N(CH_3)C(=O)-$, $-CH_2O-$, $-CH(CH_3)O-$, $C(CH_3)_2O-$ or $-CH_2CH_2-$.

10. A compound according to any one of claims 1 to 9 wherein n represents an integer 0.

11. A compound according to Claim 1 selected from:

3-(2,3-Dihydro-1'*H*-spiro[indene-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(pyridin-2-ylmethyl)propanamide ;

N,*N*-Dimethyl-3-(1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-(1,3-thiazol-4-ylmethyl)propanamide ;

3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(pyridin-2-ylmethyl)propanamide ;

(-)-3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(pyridin-2-ylmethyl)propanamide ;

3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(2-hydroxyethyl)-*N*-methyl-2-(pyridin-2-ylmethyl)propanamide ;

3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(2-methoxyethyl)-*N*-methyl-2-(pyridin-2-ylmethyl)propanamide ;

3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;

(-)-3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;

3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(2-methoxyethyl)-*N*-methyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;

3-(5-Fluoro-1-methyl-2-oxo-1,2-dihydro-1'*H*-spiro[indole-3,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(pyridin-2-ylmethyl)propanamide ;

3-(3,3-Dimethyl-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(pyridin-2-ylmethyl)propanamide ;

1-[3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-(1,3-thiazol-4-ylmethyl)propanoyl]-3-methylazetidin-3-ol ;

N,*N*-Dimethyl-3-(3-methyl-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-

(pyridin-2-ylmethyl)propanamide ;
3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(1*H*-pyrazol-1-ylmethyl)propanamide ;
(-)-3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(1*H*-pyrazol-1-ylmethyl)propanamide ;
3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(2-hydroxyethyl)-*N*-methyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;
(-)-3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(2-hydroxyethyl)-*N*-methyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;
3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(2-methoxy-2-methylpropyl)-*N*-methyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;
1-[3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-(1,3-thiazol-4-ylmethyl)propanoyl]-3-methylpyrrolidin-3-ol ;
3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-(3-hydroxy-3-methylbutyl)-*N*-methyl-2-(1,3-thiazol-4-ylmethyl)propanamide ;
3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*-methyl-*N*-(tetrahydrofuran-3-yl)-2-(1,3-thiazol-4-ylmethyl)propanamide ;
N,*N*-Dimethyl-3-(3-methyl-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-2-(1,3-thiazol-4-ylmethyl)propanamide ;
1'-[3-Azetidin-1-yl-3-oxo-2-(1,3-thiazol-4-ylmethyl)propyl]-6-fluoro-3*H*-spiro[2-benzofuran-1,4'-piperidine] ;
3-(6-Fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-[(4-methyl-1*H*-pyrazol-1-yl)methyl]propanamide;
3-(4-Chloro-1*H*-pyrazol-1-yl)-2-[(6-fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)methyl]-*N*,*N*-dimethylpropanamide;
(-)-3-(4-Chloro-1*H*-pyrazol-1-yl)-2-[(6-fluoro-1'*H*,3*H*-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)methyl]-*N*,*N*-dimethylpropanamide;
3-(6-Fluoro-3,4-dihydro-1'*H*-spiro[isochromene-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(1*H*-pyrazol-1-ylmethyl)propanamide;
3-(6-Fluoro-3,4-dihydro-1'*H*-spiro[isochromene-1,4'-piperidin]-1'-yl)-*N*,*N*-dimethyl-2-(1,3-thiazol-4-ylmethyl)propanamide;
or a pharmaceutically acceptable ester thereof.

or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition including a compound of the formula (I) or a pharmaceutically acceptable ester or salt thereof, as defined in any one of claims 1 to 11, together with a pharmaceutically acceptable excipient.

13. The use of a compound of the formula (I) or a pharmaceutically acceptable salt, solvate or composition thereof, as defined in any one of claims 1 to 11 and 12, respectively, for the manufacture of a medicament to treat a disease for which an ORL1 antagonist is indicated.

14. A use according to claim 13 where the disease is selected from pain, sleep disorders, eating disorders including anorexia and bulimia; anxiety and stress conditions; immune system diseases; locomotor disorder; memory loss, cognitive disorders and dementia including senile dementia, Alzheimer's disease, Parkinson' s disease or other neurodegenerative pathologies; epilepsy or convulsion and symptoms associated therewith; a central nervous system disorder related to gulutamate release action, anti-epileotic action, disruption of spatial memory, serotonin release, anxiolytic action, mesolimbic dopaminergic transmission, rewarding propaerties of drug of abuse, modulation of striatal and glutamate effects on locomotor activity; cardiovascular disorders including hypotension, bradycardia and stroke; renal disorders including water excretion, sodium ion excretion and syndrome of inappropriate secretion of antidiuretic hormone (SIADH); gastrointestinal disoders; airway disorders including adult respiratory distress syndrome (ARDS); autonomic disorders including suppression of micturition reflex; metabolic disorders including obesity; cirrhosis with ascites; sexual dysfunctions; altered pulmonary function including obstructive pulmonary disease; and tolerance to or dependency on a narcotic analgesic.

15. A use according to claim 13 or claim 14 where the disease is pain, sleep disorders, eating disorders including anorexia and bulimia; stress conditions; memory

loss, cognitive disorders, gastrointestinal disoders; sexual dysfunctions; tolerance to or dependency on a narcotic analgesic.

16. A method of treatment of a mammal, including a human being, to treat a disease for which an ORL1 antagonist is indicated, including treating said mammal with an effective amount of a compound of the formula (I) or with a pharmaceutically acceptable salt, solvate or composition thereof, as defined in any one of claims 1 to 10 and 11, respectively.

17. A method according to claim 16 where the disease is selected from pain; sleep disorders, eating disorders including anorexia and bulimia; anxiety and stress conditions; immune system diseases; locomotor disorder;; memory loss, cognitive disorders and dementia including senile dementia, Alzheimer's disease, Parkinson' s disease or other neurodegenerative pathologies; epilepsy or convulsion and symptoms associated therewith; a central nervous system disorder related to gulutamate release action, anti-epileotic action, disruption of spatial memory, serotonin release, anxiolytic action, mesolimbic dopaminergic transmission, rewarding propaerties of drug of abuse, modulation of striatal and glutamate effects on locomotor activity; cardiovascular disorders including hypotension, bradycardia and stroke; renal disorders including water excretion, sodium ion excretion and syndrome of inappropriate secretion of antidiuretic hormone (SIADH); gastrointestinal disoders; airway disorders including adult respiratory distress syndrome (ARDS); autonomic disorders including suppression of micturition reflex; metabolic disorders including obesity; cirrhosis with ascites; sexual dysfunctions; altered pulmonary function including obstructive pulmonary disease; and tolerance to or dependency on a narcotic analgesic.

18. A method according to claim 16 or claim 17 where the disease pain, sleep disorders, eating disorders including anorexia and bulimia; stress conditions; memory loss, cognitive disorders, gastrointestinal disoders; sexual dysfunctions; tolerance to or dependency on a narcotic analgesic.